I. Restriction requirement

Claims 11-12, 16-17 and 30-32 are canceled without prejudice in view of the restriction requirement. Claims 36-37 and 39-40 are indicated as being withdrawn from further consideration in the present application by the Examiner. However, since the Examiner included these claims in the present office action, these claims are also addressed in the response. Claims 1, 3-4, 8-10, 13-15, 28-29, 33-43 are thus pending in the application. Reconsideration of the claims is respectfully requested.

II. Claim Objection

Claim 1 is objected to because the phrase "with the substrate, and the substrate" appears redundant.

Applicants have corrected claim 1 by removing "and the substrate" to remove such redundancy. No change in scope has resulted by this deletion. Reconsideration is respectfully requested.

III. Rejection under 35 U.S.C. §112

1. On page 3 of the Office Action, claims 1, 3, 4, 8-13, 15 and 34-40 are rejected under 35 U.S.C. §112 first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention.

Applicants respectfully traverse the rejection. The support for the "antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations" is found throughout the specification, for example, at page 16, line 22 to page 17, line 4. Reconsideration is respectfully requested.

2. On page 3 of the Office Action, claims 1, 3, 4, 8-15, and 34-40 are rejected under 35 U.S.C. §112 second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

Applicants respectfully traverse the rejection. Applicants submit that since support for the "antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations" is found throughout the specification, for example, at page 16, line 22 to page 17, line 4, there is basis for these claims in the specification as filed. Therefore, the rejection of claims 1, 3, 4, 8-15, and 34-40 under 35 U.S.C. §112 second paragraph is unsupportable. Reconsideration is respectfully requested.

IV. Rejection under the judicially created doctrine of obviousness-type double patenting

On pages 3-4 of the Office Action, claims 1, 3, 4, 8-15, and 34-40 were provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over the claims of copending Application Number 09/014,087.

Applicants submit that the claims of the present application are distinct and independently patentable from the claims of copending Application Number 09/014,087. Reconsideration is respectfully requested. Additionally, Applicants will consider filing a terminal disclaimer complying with 37 CFR 3.73(b) when these claims are allowed.

V. Rejection under 35 U.S.C. §102 (b)

On page 4 of the Office Action, claims 1, 3, 4, 8, and 9 are rejected under 35 U.S.C. §102 (b) as being anticipated by Cahalan, et al. (U.S. 5,308,641).

Applicants respectfully traverse the rejection.

The Cahalan, et al. patent teaches the use of an improved spacer material and a method for making it, comprising an aminated substrate, a polyalkylimine covalently attached to the aminated substrate and a crosslinking agent. See col. 3, lines 1-20. The crosslinking agent is for crosslinking the polyalkylimine to an aminated substrate. See col. 3, lines 21-34. The polyalkylimine and crosslinking agent together formed the spacer used for improving the biocompatability of the substrate to enable the attachment of any biologically active compound to the substrate through the spacer.

See col. 4, lines 14-19. Cahalan, et al. further stresses that the spacer material intervenes between the substrate and the biologically active compound, and sometimes, a second spacer is used. See col. 4, lines 58-60, and col. 5, lines 44-55.

On the other hand, claim 1 of the present invention teaches association with or direct crosslinking of a growth factor to a substrate without a spacer material.

To anticipate a claim, the reference must teach every element of the claim. "A claim is anticipated only if each and every element as set forth in the claim is found, either expressly or inherently described, in a single prior art reference." *Verdegaal Bros. v. Union Oil Co. of California*, 2 USPQ2d 1051, 1053 (Fed. Cir. 1987). "The identical invention must be shown in as complete detail as is contained in the ... claim." *Richardson v. Suzuki Motor Co.*, 9 USPQ2d 1913, 1920 (Fed. Cir. 1989). Therefore, all claim elements, and their limitations, must be found in the prior art reference to maintain a rejection based on 35 U.S.C. §102. Applicants respectfully submit that Cahalan, et al. fail to teach either the association with or direct crosslinking of a growth factor to a substrate without a spacer material, the subject matter of claim 1. Cahalan also fails to teach associating growth factors with the substrate by antibody-antigen associations, by specific binding protein-receptor associations or by enzyme-substrate associations, to stimulate association of viable cells with the substrate. Therefore, Cahalan does not teach every element of claim 1, and therefore fails to anticipate the claims. In addition, Cahalan, et al. specifically teaches away from the association with or direct crosslinking of claim 1.

Dependent claims 3, 4, 8, and 9, which are dependent from independent claim 1, were also rejected under 35 U.S.C. §102(b) as being unpatentable over Cahalan. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 1. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 3, 4, 8, and 9 are also in condition for allowance. Applicants respectfully request that the rejection of claims 1, 3, 4, 8, and 9 under 35 U.S.C. §102 be withdrawn.

VI. Rejection under 35 U.S.C. § 103(a)

1. On page 5 of the Office Action, claims 10 and 15 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Cahalan, et al. in view of Goldstein (U.S. 5,613,982).

Applicants respectfully traverse the rejection.

Cahalan, et al. teaches attachment of a biomolecule to the spacer which is lightly crosslinked to the substrate using a crosslinking agent. Thus, Cahalan, et al. not only fails to teach association with or direct crosslinking of a growth factor to a substrate without a spacer material, it teaches away from such association or direct crosslinking. At the same time, Goldstein teaches a method of preparing a xenogeneic tissue matrix by removing native cells and other antigens from the tissue matrix. See col. 2, lines 44-63. In addition, Goldstein teaches that various enzymatic and chemical treatments to remove viable native cells from implant tissues and organs may be used. See col. 5, lines 12-19. Therefore, Goldstein also fails to teach association with or direct crosslinking of a growth factor to a substrate.

On the other hand, claim 1 of the present invention teaches association with or direct crosslinking of a growth factor to a substrate without a spacer material. This deficiency is found in both Cahalan, et al. and Goldstein.

Three criteria must be met to establish a *prima facie* case of obviousness. First, there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference. Second, there must be a reasonable expectation of success. Finally, the prior art reference, or combination of references, must teach or suggest all the claim limitations. MPEP § 2142. Since Cahalan, et al. teaches away from association with or direct crosslinking of a biologically active compound to a substrate, and Goldstein also fails to teach such association with or direct crosslinking of a growth factor to a substrate, the deficiency in Cahalan is therefore not supplied by Goldstein. Applicants respectfully traverse the rejection since the prior art fails to disclose all the claim limitations and there would be no motivation to combine the references as proposed by the Examiner.

Claims 10 and 15 are dependent from claim 1. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent claim 1. These dependent claims include all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish these claims from the cited references. Therefore, dependent claims 10 and 15 are in condition for allowance.

2. On page 6 of the Office Action, claim 13 is rejected under 35 U.S.C. § 103(a) as being unpatentable over Cahalan, et al. in view of Bayne, et al. (EP 0 476 983).

Applicants respectfully traverse the rejection.

The deficiency of Cahalan, et al., as discussed above, is also applicable here. Bayne et al teaches a vascular endothelial cell growth factor isolated and purified from glioma cell conditioned medium. See page 3, lines 46-55. The main focus of Bayne et al is on the isolation and characterization of VEGF II mammalian glioma cells. See examples. Thus, Bayne et al also fails to teach association with or direct crosslinking of a growth factor to a substrate. See page 8, lines 20-23. The deficiency in Cahalan is thus not supplied by Bayne et al. Applicants respectfully traverse the rejection since the prior art fails to disclose all the claim limitations and there would be no motivation to combine the references as proposed by the Examiner.

Claim 13 is dependent from claim 1. While Applicants do not acquiesce with the particular rejections to these dependent claims, it is believed that these rejections are moot in view of the remarks made in connection with independent 1. Dependent claim 13 includes all of the limitations of the base claim and any intervening claims, and recite additional features which further distinguish it from the cited references. Therefore, dependent claim 13 is in condition for allowance

In view of the reasons provided above, it is believed that all pending claims are in condition for allowance. Applicants respectfully request favorable reconsideration and early allowance of all pending claims.

If a telephone conference would be helpful in resolving any issues concerning this communication, please contact Applicants' attorney of record, Hallie A. Finucane at 952.253.4134.

Respectfully submitted,

Altera Law Group, LLC

Date: January 22, 2003

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Appendix A
Marked Up Version of the Entire Claim Set

The entire set of pending claims is provided for the Examiner's convenience.

1. (Eight Times Amended) A biomedical device comprising a substrate and a polypeptide growth factor associated with the substrate by covalent bonding using crosslinking agents, antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, wherein the crosslinking agents comprise at least two aldehyde functional groups that form covalent bonds to link the crosslinking agent directly with the polypeptide growth factor and the substrate, the polypeptide growth factor associated with the substrate being effective to stimulate association of viable cells with the substrate [, and the substrate].

3. (Unchanged) The biomedical device of claim 1 wherein the crosslinking agent comprises difunctional aldehydes.

4. (Unchanged) The biomedical device of claim 3 wherein the difunctional aldehyde comprises glutaraldehyde.

8. (Unchanged) The biomedical device of claim 1 wherein the substrate comprises tissue.

9. (Unchanged) The biomedical device of claim 1 wherein the substrate comprises human tissue.

10. (Unchanged) The biomedical device of claim 1 wherein the substrate is selected from the group consisting of porcine tissue, bovine tissue, kangaroo tissue, canine tissue and a combination thereof.

13. (Unchanged) The biomedical device of claim 1 wherein the polypeptide growth factor comprises vascular endothelial growth factor.

14. (Unchanged) The biomedical device of claim 1 wherein the polypeptide growth factor comprises Tat protein.

15. (Unchanged) The biomedical device of claim 1 wherein the biomedical device comprises an artificial organ, a heart valve prosthesis, an annuloplasty ring, a stent, a pledget, suture, an electrical lead, a permanently in-dwelling percutaneous device, an AV shunt, a vascular graft, a dermal graft or a surgical patch.

28. (Unchanged) A biomedical device comprising a biocompatible substrate and a polypeptide growth factor associated with the biocompatible substrate, the polypeptide growth factor being effective to stimulate association of viable cells with the substrate, wherein the polypeptide growth factor comprises Tat protein.

29. (Unchanged) The biomedical device of claim 28 wherein the biocompatible substrate comprises tissue.

33. (Unchanged) The biomedical device of claim 28 further comprising an adhesive, the adhesive being associated with the polypeptide growth factor and the substrate.

34. (Unchanged) A biomedical device comprising a substrate and a polypeptide growth factor associated with the substrate by antibody-antigen associations, specific binding protein-receptor associations or enzyme-substrate associations, the polypeptide growth factor associated with the substrate being effective to stimulate association of viable cells with the substrate.

35. (Unchanged) The biomedical device of claim 34 wherein the biocompatible substrate comprises tissue.

36. (Unchanged) The biomedical device of claim 34 wherein the biocompatible

substrate comprises a synthetic material.

37. (Unchanged) The biomedical device of claim 34 wherein the substrate comprises a bioresorbable material.

38. (Unchanged) The biomedical device of claim 34 wherein the polypeptide growth factor is associated with the substrate by antibody-antigen associations.

39. (Unchanged) The biomedical device of claim 34 wherein the polypeptide growth factor is associated with the substrate by specific binding protein-receptor associations.

40. (Unchanged) The biomedical device of claim 34 wherein the polypeptide growth factor is associated with the substrate by enzyme-substrate associations.

41. (New) A prosthesis comprising a substrate and a polypeptide growth factor associated with the substrate, the polypeptide growth factor being effective to stimulate association of viable cells with the substrate, said polypeptide growth factor comprises Tat protein.

42. (New) The prosthesis of claim 41 further comprising an adhesive, the adhesive being associated with the polypeptide growth factor and the substrate.

43. (New) The biomedical device of claim 1 comprising a crosslinking agent.